REMARKS

Claims 1-34 are presently pending in this application. Applicants have canceled claims 1-34, without prejudice, and inserted new claims 35-79. The claims have been rejected under (i) 35 U.S.C. § 112, first paragraph; and (ii) the judicially created doctrine of obviousness-type double patenting. For reasons detailed below, the rejections should be withdrawn and the claims allowed to issue.

1. The Rejection Under 35 U.S.C. §112, First Paragraph Should Be Withdrawn

Claims 1-17 are rejected under 35 U.S.C §112, first paragraph. The Examiner alleges that while the specification is enabled for producing a chimeric mRNA in a cell *in vitro*, it does not reasonably provide enablement for producing a chimeric mRNA in a cell *in vivo* for therapeutic treatment of conditions associated with defects in the coding region of the factor VIII gene.

The enablement requirement of 35 U.S.C.§112, first paragraph, requires that the specification adequately disclose to one of skill in the relevant art how to make, or in the case of a process, how to carry out, the claimed invention without undue experimentation. Process Control Corp. v. Hydroclaim Corp., 190 F.3d 1350 (Fed. Cir. 1999)

Applicants maintain that the instant specification adequately discloses how to make and use the presently claimed invention without undue experimentation. All that is required is that the teachings of the specification be followed. Specifically, the present specification clearly teaches (i) structures of pre-*trans*-splicing molecules designed to correct a factor VIII defect (section 5.1 of the specification); (ii) synthesis of pre-*trans*-splicing molecules

including cloning into eukaryotic expression vectors (section 5.2 of the specification); and methods for administering said pre-*trans*-splicing molecules (section 5.3 of the specification).

Moreover, Applicants have proven that the compositions and methods of the invention can be used to correct a factor VIII defect ***in vivo***. Indeed, working Example 12 of the specification demonstrates the successful ***in vivo*** correction of a factor VIII defect in a murine model system for hemophilia. In this regard, the Examiner's attention is respectfully directed to Figure 46 which demonstrates that factor VIII could be detected in the blood of factor VIII deficient mice following portal vein injection of PTM plasmid DNA.

Thus, given the teachings of the specification of methods for making and using pre-*trans*-splicing molecules, coupled with the successful *in vivo* use of such pre-*trans*-splicing molecules for correction of a factor VIII defect, Applicants maintain that the presently claimed invention is enabled as required by 35 U.S.C. §112, first paragraph.

2. The Claims are Rejected Under the Judicially Created Doctrine of Obviousness Double Patenting

Claims 1-34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 6,013,487. In response, Applicants will file a terminal disclaimer upon indication that claims have been allowed.

CONCLUSION

Entry of the foregoing amendments and remarks into the file history of the above-identified application is respectfully requested. Applicant believes that the foregoing amendments and remarks place the claims in condition for allowance. Withdrawal of all rejections and reconsideration of the amended claims is requested.

Respectfully submitted,

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